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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/909,464	07/19/2001	Michael Lanahan	9207-4	7251

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EXAMINER
HENDRICKS, KEITH D

ART UNIT	PAPER NUMBER
1761	

DATE MAILED: 06/28/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

9N

Office Action Summary	Application No.	Applicant(s)	
	09/909,464	LANAHAN ET AL.	
	Examiner	Art Unit	
	Keith Hendricks	1761	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-57 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-57 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 8 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 8-15, 19-23, 26-35, 39-44, 47, and 51-56, are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Further, the specification, while being enabling for the use of the alpha-galactosidase and its encoding nucleotide structure from *Thermotoga maritima*, does not reasonably provide enablement for the use of an alpha-galactosidase or its encoding nucleotide structure from either of *Thermotoga elfii* or *Thermotoga* sp. T2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicants have not provided sufficient means and/or materials for one skilled in the art to practice the claimed invention, with respect to the claims as they would be directed to the use of an alpha-galactosidase or its encoding nucleotide structure from either of *Thermotoga elfii* or *Thermotoga* sp. T2. The alpha-galactosidase from *Thermotoga* sp. T2 is not specifically disclosed as available in the instant specification, and thus provides no guidance as to where and how one skilled in the art would obtain and use this enzyme. It appears that the T2 enzyme was, at least, known in the art (for example, see Y. Koyama et al., Applied and Environmental Microbiology, 1990, vol 56: 2251-2254). However, this reference states that the "expression of the introduced alpha-galactosidase gene was not ascertained" (pg. 2253), and there is no disclosure of the isolation of the actual enzyme from *Thermotoga* sp. T2. Thus, the examiner is not aware of the public availability of the alpha-galactosidase from either *Thermotoga* sp. T2, or *Thermotoga elfii*. If applicants possess such knowledge, they are requested to present it in the subsequent response to this Office action.

A number of factors must be considered in assessing the enablement of an invention, including the following: the breadth of the claims, the amount of experimentation necessary, the guidance provided in the specification, working examples provided, predictability, and the state of the art. See *In re Wands*, 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Circ. 1988). The claims encompass the attainment and use of

alpha-galactosidase enzymes from *Thermotoga maritima, Thermotoga elfii* and *Thermotoga* sp. T2. The specification, however, provides specific guidance and working examples for such an enzyme from *Thermotoga maritima,* alone. While it is theoretically possible, and perhaps even plausible, that one skilled in the art would be able to eventually obtain the enzyme from *Thermotoga* sp. T2, or even *Thermotoga elfii*, plus further isolate the enzyme, form DNA probes for its successful expression, and subsequently use these items in the methods and products of the instant claims, this would be far removed from the teachings and enablement of the instant specification. Again, the specification does not place one skilled in the art in possession of these materials, and does not provide a sound, repeatable means by which one skilled in the art would be able to arrive at these claimed features. It is further noted that no specific claims were set forth to the sole specific use of these enzymes, nor to an "additive" composition comprising these enzymes. This could, in fact, potentially constitute a separate invention, if someday eventually isolated and enabled in a future U.S. patent application, by applicants or another entity. It is not, however, enabled in the present application, such that one skilled in the art could make and/or use that portion of the claimed invention.

Further to the point, while the conditions necessary to meet the requirements under 35 U.S.C. 112, first paragraph, are slightly different, and indeed separate, from those necessary to ascertain and meet a proper rejection under 35 U.S.C. 103(a), it is noted that a 35 U.S.C. 103(a) rejection was not made over the reference of Yernool et al. alone (cited below). Yernool et al. stated that the *Thermotoga neapolitana* nucleic acids disclosed therein, "may also be utilized as probes to identify related genes from other *Thermotoga* species" (col. 9-10), and that "such variants are considered substantially the same as one another and are included within the scope of the present invention" (top, col. 7). The denotation of the alpha-galactosidase genes and enzymes are used "to denote that they are from *Thermotoga*, but not necessarily from *Thermotoga neapolitana.*" At column 2, lines 32-33, Yernool et al. refers to the alpha-galactosidase from Thermus strain T2 (i.e. *Thermotoga* sp. T2). However, it would not be proper to assert that Yernool et al. was enabled for the specific experimentation, obtaining, culturing, enzyme isolation, DNA cloning of the corresponding gene, and subsequent use of such from all other *Thermotoga* species, including *Thermotoga maritima, Thermotoga elfii* and *Thermotoga* sp. T2. An additional reference, which demonstrated the actual isolation and use of such an enzyme from *Thermotoga maritima*, was necessary to demonstrate the availability and enablement of such a protocol.

Thus, similarly, simply because applicants have provided the names of two other known *Thermotoga* species, from which alpha-galactosidases *could* be isolated and utilized, does not render the use of such enzymes, as enabled.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 57 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 57 is directed to "an isolated edible soy protein". It is suggested that the claim be amended to recite "an edible soy protein isolate", which is a collection of soy proteins, distinct from a single "soy protein", which has been "isolated". Applicant has not disclosed or enabled the actual claimed invention, as currently recited.

Double Patenting

Claim 52 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 44. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claims 44 and 52 differ only in the recited intended use within the preamble of the claim. The substantive, physical elements of the claim are exactly the same, namely the hyperthermophilic alpha-galactosidase from one of the three recited microorganisms.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

Claim 57 is rejected under 35 U.S.C. 102(e) as being anticipated by Johnson (US PAT 5,936,069, of record).

Johnson discloses a method of "producing improved soy protein concentrate from genetically modified soybeans." The soybeans have been modified to reduce or eliminate raffinose and stachyose content, such that "little or no oligosaccharides" are present in the final product. As the product has no oligosaccharides which cause flatulence, and because the product is almost entirely protein (col. 15), "it can be used in place of soy protein isolates in many applications." Regardless of this particular feature, the reference discloses the more traditional soy protein isolate product, at column 4. It states that soy protein isolates are the most refined of the soy protein products, are "low in oligosaccharides, having negligible amounts of raffinose and less than 2% stachyose in the final product." The soy protein isolates are gel treated to remove the remaining oligosaccharides.

Thus, the reference anticipates the claim. Regardless of the mode of production, soy protein isolates with low, negligible amounts of raffinose and stachyose, were well-known in the art.

Claims 1-2, 7-8, 11-13, 15-18, 44-50 and 52 are rejected under 35 U.S.C. 102(b) as being anticipated by Liebl et al. (of record).

Liebl et al. disclose the isolation, cloning and expression of the hyperthermophilic alpha-galactosidase from *Thermotoga maritima* (DSM 3109). It had an optimum activity in the temperature range of 90-95° C. "The enzyme released galactose from raffinose" (abstract; page 6). The determination of enzymatic activity on an alpha-galactoside substrate was performed at varying temperatures, from 22-98° C (pg. 2, col. 2). "The thermoinactivation kinetics of GalA [from *Thermotoga maritima* DSM 3109] are only slightly faster than reported for the *T. neapolitana*" (pg. 8, col. 1). Page 10, col. 1, states that possible applications for thermostable alpha-galactosidases are "the elimination of raffinose from sucrose syrups in sugar beet processing." It is noted that claims 44 and 52 are directed to "additives" containing the *T. maritima* alpha-Gal enzyme, but do not contain any other components, and thus the claim limitations are met by Liebl et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yernool et al. (US PAT 6,150,171), in view of the combination of Liebl et al., and Bylina et al. (WO 98/24799).

Liebl et al. is taken as cited above.

Yernool et al. disclose the recombinant production of an alpha-galactosidase enzyme from *Thermotoga neapolitana*. "The thermostable enzyme is used in high-temperature processing of soy products to remove alpha-galactosides" (abstract; col. 1-2), acting upon raffinose and stachyose to hydrolyze them to their constituent sugars, including galactose (col. 11, 16). Such "enzymatic processes could be commercially competitive by using highly thermostable enzymes with sustained activity above 80° C" (col. 2). "The alpha-galactosidase encoded by this nucleic acid molecule has an optimum temperature of activity of between about 84° C and 100° C" (col. 3). "Generally, the methods comprise heating the soy products to a temperature at least as high as about 65-70° C (preferably 70-105° C, depending on the length of heating and other specifics of the material being heated)". This method is also applicable to other legume products (col. 4). Yernool et al. states that the *Thermotoga neapolitana* nucleic acids disclosed therein, "may also be utilized as probes to identify related genes from other *Thermotoga* species" (col. 9-10), and that "such variants are considered substantially the same as one another and are included within the scope of the present invention" (top, col. 7). The denotation of the alpha-galactosidase genes and enzymes are used "to denote that they are from *Thermotoga*, but not necessarily from *Thermotoga neapolitana*." "The *Thermotoga* alpha-galactosidase of the invention can be used for any purpose for which alpha-galactosidase is used" (col. 10). For example, soy meal can be heat-treated, along with the addition of the thermostable alpha-galactosidase "to produce feeds that can be fed to non-ruminants, such as chicken and pigs." "The use of the alpha-galactosidase in this step further improves the digestibility and nutritional quality of the feed. Both normal and de-fatted soy products may be utilized (bottom, col. 10). The alpha-gal. enzyme may also be used "in any heated, cooked or baked product in which soy meal or defatted soy flour is presently used", as well as with soy milk and soy yogurt (col. 10-11). Another use for the thermostable alpha-galactosidase is in the hydrolysis of raffinose

in sugar beets, into its constituent sugars of galactose and sucrose (col. 11). While the enzyme was stated to be used "between about 84° C and 100° C" for the hydrolysis of flatulence-causing oligosaccharides, it had a temperature optimum of 93° C (col. 16).

Bylina et al., at page 2, disclose that alpha-galactosidases may be used to eliminate raffinose in beets, and "has also been used as a digestive aid to break down raffinose, stachyose and verbascose in such foods as beans and other gassy foods." Figure 10 and SEQ ID NOs: 10 and 24 contain the polynucleotide and amino acid sequence for the alpha-galactosidase from *Thermotoga maritima* MSB8 (DSM 3109). See also pages 11, 32 and 35. Claims 9 and 10 of the reference describe a method for generating glucose by hydrolyzing soluble cell oligosaccharides in such items as dairy products, fruit juices, animal feed, and plant biomass, with one of the enzymes disclosed, including the *T. maritima* alpha-galactosidase.

Thus, it would have been obvious to one of ordinary skill in the art to have utilized the known *Thermotoga maritima* alpha-galactosidase enzyme, within known processes for hydrolyzing stachyose, raffinose or verbascose in plant matter, such as that described by Yernool et al., with respect to the alpha-Gal enzyme from *Thermotoga neapolitana*. Yernool et al. disclose the advantages of using hyperthermophilic alpha-galactosidases to hydrolyze oligosaccharides to galactose, under extreme heat conditions which would otherwise denature heat-labile enzymes. The use of such alpha-Gal enzymes for the improved heat-stabile hydrolysis of oligosaccharides, in the production of animal feeds, soy products, and "human foods", were all disclosed and suggested by the references, as provided above.

Regarding the moisture content of the claimed reactions, it is noted that Yernool et al. disclose the use of the thermostable alpha-Gal with various substrates, including in culture medium, crude soy meal or moistened soy meal slurry, soy milk and soy yogurt (col. 10-11, for example). Thus, it is shown that such alpha-Gal enzymes function over a wide range of moisture contents, which would be expected to include 25%, 45% and 70%. Regarding the liquid or solid forms of the enzyme, Yernool disclosed the isolation of the enzyme, its use as partially-purified on soy molasses, and also its use in culture medium (col. 15-16). It would not have involved an inventive step in the art to have provide the *T. maritima* alpha-Gal enzyme in liquid or dry form for such known uses (for example, instant claims 39-40), as these forms were commonly practiced and provided in the art. Yernool et al. discloses that the thermostable alpha-Gal enzyme from *Thermotoga neapolitana* has activity up to and including 100° C (col. 3), and further, "generally, the methods comprise heating the soy products to a temperature at least as high as about 65-70° C (preferably 70-105° C...)." Liebl et al. disclose that the thermo-kinetics, activity and stability of the *T. maritima* alpha-galactosidase enzyme was very close to that of *T. neapolitana*. Thus, one of ordinary

skill in the art would readily have expected, and been motivated, to utilize the enzyme within the instantly-claimed ranges between 80° C and 100° C. The use of the recombinant enzyme, versus the naturally-occurring isolated enzyme, would not have differed in the actual method or product, as the enzymes would be the same, regardless of mode of production. It is noted that the instantly-claimed SEQ ID's are drawn to the alpha-Gal of *T. maritima*, and were disclosed in the art by both secondary references of Liebl et al. and Bylina et al.

Conclusion

NOTE: The claimed species as directed to the use of the alpha-galactosidases from *Thermotoga elfii* and *Thermotoga* sp. T2, are free of the prior art of record. However, the above rejection under 35 USC 112, 1st paragraph, is again noted. Despite the knowledge of the existence of a cloned alpha-galactosidase gene from *Thermotoga* sp. T2 (Koyama et al., ibid), the expression of the gene product was not detected (pg. 2253), nor was there any disclosure of the actual isolated enzyme, natural or recombinant, in this or any other publication available to the examiner. Further, there was no suggestion in the art to utilize this enzyme as instantly claimed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Keith Hendricks whose telephone number is (703) 308-2959. The examiner can normally be reached on M-F (8:30am-6pm); First Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Milton Cano can be reached on (703) 308-3959. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9310 for regular communications and (703) 872-9565 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0661.

KEITH HENDRICKS
PRIMARY EXAMINER